

Amendments

IN THE CLAIMS

Please cancel claims 1-13 and 16-29 without prejudice or disclaimer. Please add the new claims 35-62 as set forth below.

Claims 1-34 (Canceled)

35. (New) A transgenic mouse comprising human Ig lambda genes in which the proportion of the κ and λ light chains expressed by said transgenic mouse resembles that found in humans, and exhibits relative proportions of $\leq 60\%$ κ light chains and $\geq 40\%$ λ light chains.
36. (New) The transgenic mouse according to claim 35, comprising as a translocus a yeast artificial chromosome (YAC) of about 410 Kb, wherein the YAC contains at least a majority of the human $V\lambda$ genes of cluster A and all the human $J\lambda$ - $C\lambda$ segments in germline configuration, and wherein the translocus shows high expression and is able to compete with the endogenous mouse κ locus.
37. (New) The transgenic mouse according to claim 35, comprising as a translocus a YAC of about 410 Kb, wherein the YAC contains at least a majority of the human $V\lambda$ genes of cluster A and all the human $J\lambda$ - $C\lambda$ segments in germline configuration, and wherein the mouse has one or both endogenous $Ig\kappa$ alleles disrupted, and wherein the translocus shows high expression.

38. (New) The transgenic mouse according to claim 35, comprising a 380 Kb region of the human immunoglobulin (Ig) λ light (L) chain locus in germline configuration, wherein the 380 Kb region resides on a yeast artificial chromosome (YAC) that accommodates the most proximal V (variable gene) λ cluster, wherein the 380 Kb regions has 15 V λ genes and all J λ - C λ segments with the 3' region, wherein the 3' region includes a downstream enhancer.
39. (New) The transgenic mouse according to claim 35, wherein the mouse includes a Hulg λ YAC that accommodates a 380 Kb region of the human λ light chain locus in authentic configuration with all V λ genes of cluster A, the J λ - C λ segments and the 3' enhancer.
40. (New) The transgenic mouse according to claim 39, wherein the Hulg λ YAC is shown in Figure 1.
41. (New) A method for producing a transgenic mouse according to claim 35, comprising:
- (a) introducing a Hulg λ YAC into murine embryonic stems cells; and
 - (b) deriving a transgenic mouse from the cells of step (a) by blastocyte injection to form a chimeric animal and then breeding the chimeric mouse to obtain a transgenic mouse.

42. (New) The method of claim 41, wherein a Hulg λ YAC of about 410Kb that can accommodate a 380 Kb region (V λ - JC λ) of the human λ light chain locus with V, J and C genes in germline configuration is introduced into said stem cells.
43. (New) The method according to claim 41 wherein two copies of the neomycin resistance gene (NEO^r) are site-specifically integrated into the ampicillin gene on the left (centromeric) YAC arm in order to permit selection.
44. (New) The method according to claim 41, wherein YAC-containing yeast cells are fused with HM-1 embryonic stem (ES) cells and G418 resistance colonies are picked and analysed 2-3 weeks after protoplast fusion.
45. (New) The method according to claim 41, wherein ES cells containing a complete Hulg λ YAC copy are used for blastocyte injection to produce a chimeric animal.
46. (New) The method according to claim 45, wherein breeding of a chimeric animal with a Balb/c mouse results in germline transmission.
47. (New) The method according to claim 46, comprising breeding the mouse with $\kappa^{-/-}$ mice to establish lines of transgenic mice.

48. (New) A transgenic mouse comprising and expressing human λ light chain locus genes and endogenous κ light chain locus genes, wherein the expression of the human λ light chain locus is equal to or greater than that of the endogenous κ light chain locus.
49. (New) The transgenic mouse comprising human λ light chain genes according to claim 48, wherein the mouse further comprises a human κ light chain locus and wherein expression of the human λ light chain locus is equal to or greater than that of the human κ light chain locus.
50. (New) The transgenic mouse carrying human λ light chain genes according to claim 48, wherein the λ translocus has been bred to homozygosity.
51. (New) The transgenic mouse carrying human λ light chain genes according to claim 48, wherein the rearranged variable genes in the λ translocus are subject to somatic hypermutation.
52. (New) The transgenic mouse carrying human λ light chain genes according to claim 48, wherein the mouse comprises as a translocus a yeast artificial chromosome (YAC) of greater than 100Kb which contains a proportion of the human $V\lambda$ genes proximal to the $J\lambda$ - $C\lambda$ cluster in germline configuration.

53. (New) The transgenic mouse according to claim 52, wherein the YAC includes a 380 Kb region of the human Ig λ locus in authentic configuration with at least a majority of the V λ genes of cluster A, J λ -C λ segments and a 3' enhancer.
54. (New) The transgenic mouse carrying human λ light chain genes according to claim 52, wherein the transgenic mouse comprises variable, joining and constant genes of the human λ light chain locus as a transgenic locus on a YAC, wherein B cells of said mouse rearranges said λ light chain genes and the mouse expresses serum immunoglobulins containing human λ light chains.
55. (New) The transgenic mouse comprising human λ light chain genes according to claim 52, wherein the λ translocus is rearranged with similar efficiency as endogenous mouse κ and at the same time as or before the endogenous κ locus.
56. (New) The transgenic mouse comprising human λ light chain genes according to claim 52, wherein the endogenous κ locus has been silenced, and the mouse expresses serum immunoglobulins containing human λ light chains.
57. (New) The transgenic mouse carrying human λ light chain genes according to claim 52, further comprising human heavy chain genes as a second transgenic locus integrated on a separate YAC, wherein the mouse expresses serum

immunoglobulin molecules containing combinations of human heavy and λ light chains.

58. (New) The transgenic mouse carrying human λ light chain genes according to claim 57, wherein the second transgenic locus carries a diversity of human heavy chain constant region genes and includes μ , δ and γ genes.
59. (New) The transgenic mouse carrying human λ light chain genes and human heavy chain genes according to claim 58, wherein the heavy chain transgenic locus carries a diversity of human heavy chain constant region genes and includes μ , δ and γ genes, wherein the heavy chain constant regions genes are in authentic germline configuration.
60. (New) The transgenic mouse carrying human λ light chain genes according to claim 52, further comprising human κ light chain genes as a second transgenic light chain locus integrated on a separate YAC, wherein the mouse expresses serum immunoglobulin molecules containing human κ and λ light chains.
61. (New) The transgenic mouse carrying human λ light chain genes according to claim 52, further comprising human heavy chain genes as a second transgenic locus and human κ light chain genes as a third transgenic locus, wherein the mouse expresses serum immunoglobulin molecules containing human heavy chains in combination with at least one of human κ or λ light chains.

62. (New) The transgenic mouse carrying human λ light chain genes according to claim 52, wherein expression of the endogenous mouse heavy and/or light chain loci has been prevented and which expresses serum immunoglobulin containing human heavy and/or light chains, wherein the transgenic mouse is deficient in production of mouse immunoglobulin.